

Genes, Genomes & Genetics Integrated Review Group (IRG)

By consensus vote of the Genetics Study Section Boundaries Team, the Genes, Genomes & Genetics (GGG) IRG is recommended to replace two IRGs proposed by the Panel on Scientific Boundaries for Review, IRG 2 Molecular Approaches to Gene Function and IRG 4 Fundamental Genetics and Population Biology. The proposed GGG IRG will review research applications that focus broadly on fundamental and applied aspects of genes, genomes and genetics of humans and a variety of other organisms.

Areas considered are fundamental mechanisms of molecular genetics, including the regulation of DNA and RNA metabolism, chromosome function and maintenance, and gene expression. Genomic studies, computational biology and technology development will also be considered, including development of new genetic tools and resources, global analysis of genetic systems, biological and computational resource development, and classification, storage, access, analysis and integration of genetic and other biological information. Genetic variation and evolution will be reviewed under the GGG IRG including the description, analysis and modeling of induced and natural genome variation, and comparisons between species. All aspects of quantitative genetics including complex trait mapping will be considered in humans and a wide variety of other species. The involvement of genetics in human health and disease will be considered, including the discovery, application and interpretation of gene and genomic variation influencing phenotype and the development of experimental and computational approaches to the identification of disease-related genes. Proposals dealing with model systems of all organisms, as they relate to human health and disease, will be considered, as will translational genetic studies applying fundamental genetic insight into the clinical setting.

The following study sections, each of which would review research project grant applications (e.g., R01s), are recommended for inclusion in the GGG IRG:

- Molecular Genetics A (MGA)
- Molecular Genetics B (MGB)
- Molecular Genetics C (MGC)
- Genomics, Computational Biology & Technology (GCAT)
- Genetic Variation & Evolution (GVE)
- Genetics of Health & Disease (GHD)

Molecular Genetics A, B, & C

The Molecular Genetics study sections will review applications on mechanisms and regulation of DNA metabolism, chromosome function and maintenance, and gene expression. While emphasis is on eukaryotic organisms, crosscutting studies involving prokaryotic systems may also be assigned to these study sections. Experimental approaches may include the use of cell-free, cell-culture, and whole organism studies, structural analyses, genomic technologies, chemical genetics, and informatics.

Specific Areas Covered by all three study sections include:

- DNA replication and cell cycle control
- DNA repair pathways
- Recombination
- Mutagenesis
- Chromosome dynamics
- Chromatin structure and remodeling

- Transcription mechanism and regulation
- Gene regulatory networks
- RNA processing and stability
- RNP (ribonucleoprotein) assembly, nuclear transport, and localization
- Non-coding RNA
- Protein synthesis and translational control
- Post-translational modifications and processes
- Protein ubiquitinylation and degradation

Areas of emphasis include:

MGA

- extrachromosomal and organelle genetics
- mobile genetic elements
- non-nucleic acid-based inheritance

MGB

- imprinting
- dosage compensation
- epigenetic processes

MGC

- chromosome structure
- meiosis and segregation
- cytogenetics

Shared Interests Within the IRG

- Genomics, Computational Biology & Technology (GCAT): Studies that apply high-throughput technologies, computational methods, and/or mathematical modeling approaches to processes covered by the Molecular Genetics study sections could be assigned to MG-A, -B, or -C as appropriate. Development of new high-throughput technologies, computational methods, network modeling, or mathematical approaches or techniques may be more appropriate for assignment to GCAT.
- Genetic Variation & Evolution (GVE): Studies addressing mechanistic questions about mutation, recombination, and chromosome dynamics could be directed to MG-A, -B, or -C as appropriate. Studies with emphasis on evolutionary aspects, including statistical methods, could be directed to GVE.
- Genetics of Health and Disease (GHD): Cytogenetic studies relating to diagnosis or disease processes could be assigned to GHD. Studies that address fundamental questions about chromosome structure and organization could be assigned to MG. Studies on imprinting, X-inactivation, organelle genetics, recombination and DNA repair could be assigned to GHD if the emphasis is on genetic disease, and applications with a distinct human genetic focus could be assigned to GHD. If the focus is on molecular mechanisms, the application could be assigned to MG.

Shared Interests Outside of the IRG

The MG study sections have shared interests in the study of genetic mechanisms with many IRGs. Applications that focus on fundamental mechanisms and/or regulation of DNA metabolism or gene expression could generally be assigned to MG-A, -B, or -C. Studies that employ a particular organ, system or disease as a model for investigating basic genetic processes may be appropriate for MG.

- IRG 1: Biological Chemistry & Macromolecular Biophysics: Shared interests include protein-nucleic acid interactions, nucleic acid enzymology, and structure/function studies of related macromolecular complexes. If the emphasis is on enzyme kinetics, detailed chemical reaction mechanisms, or high-resolution structure determination, the application could be assigned to IRG 1. If structural analysis is one of several approaches to elucidate molecular genetic mechanisms, assignment could be to MG-A, -B, or -C.
- IRG 3: Molecular Approaches to Cell Function & Interactions: Shared interests include chromosome duplication and dynamics, nucleocytoplasmic trafficking, and signal transduction pathways. If the focus is on molecular genetic mechanisms and/or regulation of DNA metabolism or gene expression, studies on nuclear transport, cell cycle control, apoptosis, and signaling pathways may be assigned to the MG-A, -B, or -C study sections. Studies focusing on mitotic processes or on cytoskeletal or nuclear envelope assembly and dynamics may be assigned to IRG 3.
- IRG 5: Biology of Development & Aging: Shared interests include cell differentiation and cell fate determination. Studies on fundamental molecular genetic questions of broad biological significance could be assigned to MG. Studies on genetic control of development and aging could be assigned to IRG 5.
- IRGs 11 & 12: Infectious Diseases & Microbiology and AIDS & Related Research: Fundamental molecular genetic studies of prokaryotic and eukaryotic organisms, including host-microbe interactions, could generally be assigned to MG, but may also be assigned to IRGs 11 or 12 particularly when the organism is pathogenic or serves as a model system for pathogenic eukaryotes.
- IRG 13: Oncological Sciences: Molecular genetic studies of cancer etiology, tumor pathogenesis, or organ-specific carcinogenesis could be assigned to IRG 13. Basic mechanistic studies of genetic processes governing eukaryotic cell growth control and cell differentiation could be assigned to MG-A, -B, or -C.
- Organ/disease IRGs (14-20): Hematology, Cardiovascular Sciences, Endocrinology, Metabolism, Nutrition, & Reproductive Sciences, Musculoskeletal, Oral, & Skin Sciences, Digestive Sciences, Pulmonary Sciences, and Renal & Urologic Sciences: Assignment of a molecular genetics application to an organ-system/disease IRG or to MG-A, -B, or -C should be based on the nature of the scientific question(s) being addressed. Studies directed at a single organ-system or disease could be assigned to the organ system or disease IRG, even if basic approaches are used. Assignment could be to the MG-A, -B, or -C if the question(s) addressed may be applicable to multiple diseases or organ systems, or if the study involves an emerging approach for which expertise resides in a MG study section.
- Neuroscience IRGs (22-24): Molecular, Cellular & Developmental Neuroscience, Integrative, Functional, & Cognitive Neuroscience, and Brain Disorders & Clinical Neuroscience: Applications with a primary focus on molecular genetic processes could be reviewed by the MG-A, -B, or -C study sections. However, applications with a primary focus on neuroscience processes could be reviewed by IRGs 22-24. The distinction is whether neuroscience questions are being asked or whether the nervous system is being used as a convenient model.

Genomics, Computational Biology and Technology (GCAT)

The Genomics, Computational Biology and Technology study section will consider research applications involving global and integrative analyses of biological systems, and the development of new computational and experimental methodologies. These would include (1) large-scale projects providing genetic information or resources that can be leveraged by the scientific community, (2) the development and application of bioinformatics and computational methods for collection, storage, integration, analysis, modeling and dissemination of genetic information, and (3) the development and validation of new experimental technologies potentially applicable to systematic analyses. These projects may pertain to humans or model systems.

Specific Areas Covered

- Large-scale gene/protein/metabolite analyses (e.g., microarrays, proteomics, genomics, metabolomics, genome sequencing, gene identification, network construction, chemical genetics)
- Large-scale genetic resources (e.g., collections of mutant strains and lines, tagged genes, small molecule probes)
- Comprehensive studies of specific systems (e.g., cell cycle, signal transduction, metabolic control, disease pathways)
- Technology development for understanding simple and complex systems (single gene/protein as well as high throughput approaches)
- Computational and mathematical representation and simulation of genetic systems (e.g., genetic networks, metabolic networks, protein networks, signaling, physiology, host-pathogen interactions)
- Analysis, mining, and integration of genetic data, including the development of new algorithms
- Classification and annotation systems for genetic data
- Data storage, databases, and access to information (e.g., user interfaces)
- Development of model organisms/systems for genetic, genomic, or high-throughput analyses

Shared Interests Within the IRG

In general the GCAT study section could review applications pertaining to new and emerging technologies, large-scale/high throughput studies, and computational modeling of genetic systems. Applications using established technologies applied to specific problems should be reviewed by other study sections.

- Molecular Genetics A, B, or C (MG-A, -B, or -C): Studies that apply high-throughput technologies, computational methods, and/or mathematical modeling approaches to processes covered by the Molecular Genetics study sections could be assigned to MG-A, -B, or -C as appropriate. Development of new high-throughput technologies, computational methods, network modeling, or mathematical approaches or techniques could be assigned to GCAT.
- Genetic Variation & Evolution (GVE): If studies are directed principally at understanding evolutionary processes or gene and genome evolution, including statistical methods, they could be assigned to GVE. If studies are directed at new and emerging genetic technologies, high throughput efforts, or computational modeling of genetic systems, they could be assigned to GCAT.
- Genetics of Health & Disease (GHD): Proposals applying workable technologies and approaches to diseases on the human or model genome-scale are appropriate for assignment to the GHD study section. Development of genomic technologies and global approaches are appropriate for assignment to the GCAT study section.

Shared Interests Outside of the IRG

- Basic and crosscutting IRGs (1, 3, & 5): Projects reviewed by GCAT may be pertinent to all areas of biology. For example, IRG 1: Biological Chemistry and Macromolecular Biophysics, IRG 3: Molecular Approaches to Cell Function and Interactions and IRG 5: Biology of Development & Aging will cover topics related to the basic analysis of gene function, and other IRGs will cover aspects of genomics, proteomics, computational biology and technology related to specific organs and diseases. GCAT could review applications pertaining to new and emerging technologies, large-scale/high throughput studies, and computational modeling of genetic systems. Applications using established technologies applied to specific problems should be reviewed by other IRGs.
- IRG 6: Bioengineering Sciences & Technologies (BST): Bioinformatics and database proposals may be reviewed in GCAT and in the BST's Biodata Management & Analysis and Modeling and Analysis of Biological Systems study sections. Research that is linked to genetic problems could be reviewed by GCAT, whereas proposals that are more broadly oriented or where application is unknown could be reviewed by the BST IRG. Instrumentation and technology development is also reviewed by BST's Instrumentation and Systems Development study section. Technologies focusing on global analyses of gene/genomic/genetic information could be assigned to GCAT. This would include initial development applications as well as their application in a systematic fashion. Proposals that have a focus on complex bioengineering technologies could be reviewed by BST.
- Health of the Population IRG 7: Applications with a focus on gene/genomic/genetic technologies could be reviewed by the GCAT study section. However, applications with a primary focus on genetic epidemiology could be reviewed by IRG 7.
- Organ/disease IRGs (14-20): Hematology, Cardiovascular Sciences, Endocrinology, Metabolism, Nutrition, & Reproductive Sciences, Musculoskeletal, Oral, & Skin Sciences, Digestive Sciences, Pulmonary Sciences, and Renal & Urologic Sciences: Assignment of a gene/genomics/genetics application to an organ-system/disease IRG or to GCAT should be based on the nature of the scientific question(s) being addressed. Studies directed at a single organ-system or disease could be assigned to the organ system or disease IRG, even if basic approaches are used. Assignment could be to GCAT if the question(s) addressed may be applicable to multiple diseases or organ systems, or if the study involves an emerging approach for which expertise resides in GCAT.
- Neuroscience IRGs (22-24): Molecular, Cellular & Developmental Neuroscience, Integrative, Functional, & Cognitive Neuroscience, and Brain Disorders & Clinical Neuroscience: Applications with a focus on gene/genomic/genetic technologies could be reviewed by the GCAT study section. However, applications with a primary focus on neuroscience processes could be reviewed by IRGs 22-24.

Genetic Variation and Evolution (GVE) Study Section

The GVE study section addresses grant applications related to the origin, distribution, maintenance, and effects of genetic variation. It considers studies ranging from characterization of the genetic and phenotypic differences among individuals and species to the evolution of genomes and biological systems.

Topics of interest include (but are not limited to):

- Description and modeling of the levels and patterns of variation
- Analysis of induced and natural variation for Mendelian and complex traits
- Genotype-phenotype associations
- Use of natural variation for gene discovery and functional genomics
- Genetics of speciation
- Adaptive evolution
- Chromosome evolution

- Evolution and organization of genomes, including gene duplication, repetitive elements, and multigene families
- Evolution of gene regulation and regulatory circuits
- Evolution of development
- (Co) evolution of hosts and their symbionts/pathogens
- Genetic variation and environmental factors

These topics will be investigated in a variety of species, including humans, other animals, plants, and microbes. Approaches include molecular genetics; quantitative trait locus analysis, linkage and association mapping; experimental and theoretical population genetics; experimental or simulated evolution; phylogenetics; molecular evolutionary analysis; comparative genomics; gene expression and protein analyses.

GVE may welcome applications that attempt to dissect complex morphological, behavioral, physiological and fitness-related phenotypes. Proposals to be considered may also include the development of statistical methods for inferring evolutionary processes or mapping quantitative traits; development of new model systems relevant to these topics; community-wide resources, such as database and computational tools; and modeling the emergence of naturally occurring or intentionally released infectious diseases, including genetic, evolutionary and ecological mechanisms and interactions.

Shared Interests Within the IRG

- Molecular Genetics-A, -B, & -C (MG-A, -B, & -C): Studies addressing mechanistic questions about mutation, recombination, and chromosome dynamics could be directed to MG-A, -B, or -C as appropriate. Studies with emphasis on evolutionary aspects could be directed to GVE.
- Genomics, Computational Biology & Technology (GCAT): If studies are directed principally at understanding evolutionary processes or gene and genome evolution, they could be assigned to GVE. If studies are directed at new and emerging genetic technologies, high throughput efforts, or computational modeling of genetic systems, they could be assigned to GCAT.
- Genetics of Health & Disease (GHD): Genetic variation, modeling human history, comparative genomics, and complex trait mapping are shared interests. GVE may be appropriate for applications emphasizing evolutionary aspects of complex trait analysis, comparative genomics, and development of experimental, statistical, and theoretical methods. GHD may be more appropriate for proposals emphasizing human variation in disease.

Shared Interests Outside of the IRG

- IRG 5: (Biology of Development and Aging): Shared interests are in the study of the genetic variation of aging and the evolution of development. If the primary focus is to characterize natural variation or test evolutionary models or to elucidate evolutionary processes, applications could be assigned to GVE. Applications using established genetic technologies applied to specific aging problems could be assigned to IRG 5.
- IRG 6: (Bioengineering Sciences & Technologies): Shared interests include computational methods and informatics. Proposals specifically addressing statistical and computational methods for the analysis of genetic variation could be reviewed by GVE. Proposals that are more broadly oriented or where application is unknown could be reviewed by the BST IRG.
- IRG 10: (Immunology): Proposals specifically addressing genetic and phenotypic variation in immune response could be reviewed by GVE. Applications using established genetic technologies applied to specific immunological problems could be reviewed by IRG 10.

- IRGs 11 and 12: Infectious Diseases & Microbiology and AIDS & Related Disorders: Proposals specifically addressing genetic variation and evolution of infectious agents could be reviewed by GVE. Applications using established genetic technologies applied to specific infectious agents could be reviewed by IRGs 11/12.
- Organ/disease IRGs (14-20): Hematology, Cardiovascular Sciences, Endocrinology, Metabolism, Nutrition, & Reproductive Sciences, Musculoskeletal, Oral, & Skin Sciences, Digestive Sciences, Pulmonary Sciences, and Renal & Urologic Sciences: Assignment of a genetic analysis of complex traits application to an organ-system/disease IRG or to GVE should be based on the nature of the scientific question(s) being addressed. Studies directed at a single organ-system or disease could be assigned to the organ system or disease IRG, even if basic approaches are used. Assignment could be to GVE if the question(s) addressed may be applicable to multiple diseases or organ systems, or if the study involves an emerging approach for which expertise resides in GVE. Thus, proposals mapping genes affecting variation in complex traits could be considered by GVE; applications emphasizing functional and mechanistic studies could be assigned to the appropriate disease or organ system IRG.
- Neuroscience IRGs (22-24): Molecular, Cellular & Developmental Neuroscience, Integrative, Functional, & Cognitive Neuroscience, and Brain Disorders & Clinical Neuroscience: Applications with a focus on genetic variation or evolution could be reviewed by the GVE study section. However, applications with a primary focus on neuroscience processes could be reviewed by IRGs 22-24.

Genetics of Health and Disease (GHD)

The GHD Study Section will review applications involving the discovery, application and interpretation of genetic and genomic variation in human phenotype and disease.

Specific Areas Covered

- Genetic basis of Mendelian and non-Mendelian human diseases
- Mapping and identification of normal and disease phenotypes, including those associated with rare disorders
- Genetic and epigenetic phenomena such as imprinting, X inactivation, repeat expansions, genetic recombination and DNA repair, where genetic disease is emphasized
- Non-Mendelian traits including mitochondrial and organelle diseases
- Quantitative genetics of complex traits, genetic dissection, including QTL (quantitative trait locus) mapping
- Disease-related variations including SNPs (single nucleotide polymorphisms) and haplotypes
- Cytogenetics and chromosome disorders
- Genome architecture and genomic disorders
- Pharmacogenetics and biochemical genetics, including inborn errors of metabolism
- Interaction of the genome with exogenous factors including environment and maternal genotype
- Models of human diseases, including, but not limited to, mouse, *Drosophila*, zebra fish, *Caenorhabditis elegans*, yeast, and other organisms
- Genetic, pre-implantation and prenatal diagnostics
- Therapeutic approaches to genetic disease including gene and protein replacement therapy
- Translational genetics, including outcome studies concerning genotype-phenotype correlation and the application of fundamental genetics to clinical practice

- Genetic epidemiology, population and newborn screening, and public health applications of genetics
- Genetic counseling and education
- Ethical and social issues in genetics

Shared Interests Within the IRG

- Molecular Genetics-A, -B, & -C (MG-A, B, & -C): Cytogenetic studies relating to diagnosis or disease processes could be assigned to GHD. Studies that address fundamental questions about chromosome structure and organization could be assigned to MG. Studies on imprinting, X-inactivation, organelle genetics, recombination and DNA repair could be assigned to GHD if the emphasis is on genetic disease. If the focus is on molecular mechanisms, such applications could be assigned to MG.
- Genomics, Computational Biology & Technology (GCAT): Proposals applying workable technologies and approaches for diseases on the human or model genome-scale, are appropriate for assignment to the GHD study section. Development of genomic technologies and global approaches are appropriate for assignment to the GCAT study section.
- Genetic Variation & Evolution (GVE): Genetic variation, modeling human history, comparative genomics, and complex trait mapping are shared interests. GVE may be appropriate for applications emphasizing evolutionary aspects of complex trait analysis, comparative genomics, and development of experimental, statistical, and theoretical methods. GHD may be more appropriate for proposals emphasizing human variation in disease.

Shared Interest Outside of the IRG

- Health of the Population IRGs 7: Applications with a focus on gene/genomic/genetic disease could be reviewed by the GHD study section. However, applications with a primary focus on genetic epidemiology could be reviewed by IRG 7.
- Neuroscience IRGs (22-24): Molecular, Cellular & Developmental Neuroscience, Integrative, Functional, & Cognitive Neuroscience, and Brain Disorders & Clinical Neuroscience: Applications with a focus on gene/genomic/genetic disease could be reviewed by the GHD study section. However, applications with a primary focus on neuroscience processes could be reviewed by IRGs 22-24. Thus, proposals focusing on gene discovery and the genetic dissection of non-Mendelian human diseases and traits using complex or novel technologies may be more appropriate for GHD, while those using established genetic methods to study Mendelian diseases or complex diseases and traits where a specific gene unambiguously has been identified may be more appropriate for other IRGs.
- Other IRGs (5, 10, and 13-20): Biology of Development & Aging, Immunology, Oncological Sciences, Hematology, Cardiovascular Sciences, Endocrinology, Metabolism, Nutrition, & Reproductive Sciences, Musculoskeletal, Oral, & Skin Sciences, Digestive Sciences, Pulmonary Sciences, and Renal & Urologic Sciences: Assignment of a genetic disease application to an organ-system/disease IRG or to GHD should be based on the nature of the scientific question(s) being addressed. Studies directed at a single organ-system or disease could be assigned to the organ system or disease IRG if the focus is primarily on the elucidation of specific known disease mechanisms, molecules, or pathways. Assignment could be to GHD if the study uses molecular or other methods for gene discovery in complex, non-Mendelian diseases, or if the study involves an emerging approach for which expertise resides in GHD. Thus, proposals focusing on gene discovery and the genetic dissection of non-Mendelian human diseases and traits using complex or novel technologies may be more appropriate for GHD, while those using established genetic methods to study Mendelian diseases or complex diseases and traits where a specific gene unambiguously has been identified may be

more appropriate for other IRGs (e.g., cancer genetics study section in IRG 13, CMAD in IRG 5, GCMB in IRG 18, CMI in IRG 10, CMBK in IRG 20, MCE and CADO in IRG 16).